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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,020	03/27/2003	Amarjit Singh	U 013943-5	9010

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EXAMINER	
PRYOR, ALTON NATHANIEL	
ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
01/27/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/089,020	SINGH ET AL.	
	Examiner	Art Unit	
	ALTON N. PRYOR	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,8-11,19,25 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *26* is/are allowed.

6)☒ Claim(s) *1,5,8-11,19 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed 11/4/10 have been fully considered but they are not persuasive. See argument below. Rejections and objections not recited below are withdrawn. An Appeal conference was held and it was decided that the claims are allowable once the 103 and 112 rejections are cleared with respect to the scope of the sustain release biodegradable materials claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1,5,8-11,19 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skinhoj et al (US 6599529; 7/29/03), Saslawski et al. (WO 99/33448; 7/8/99) in view of Gibson et al. (US 6426340; 7/30/02) based on US Provisional 60/018202; 5/23/96). Skinhoj et al teach a once a day oral pharmaceutical modified release multiple-units formulation (column 21 lines 34-53) comprising NSAID compounds including nimesulide and naproxen (claim 9). Skinhoj et al teach two fractions of multiple units wherein both fractions contain the about 5% to about 50% NSAID (column 11 lines 1-10). Skinhoj et al teach that the first fraction can contain sodium carbonate (column 20 lines 10-31). Skinhoj et al teach that individual units containing the NSAID are coated with 1-20% coating (column 22 lines 32-53). The film forming agents include ethylcellulose and colloidal silica (column 22 line 66 - column 23

line 12). The coating is an admixture of excipients and colloidal silicium dioxide (column 23 lines 57-60). The coating for the outer second layer may comprise substances such as ethylcellulose, and hydroxypropyl metthylcellulose (column 24 lines 15-44). Surfactant such as sodium lauryl sulfate can be included in the composition (column 25 lines 37-48). Skinhoj et al. do not exemplify invention comprising nimesulide in both the immediate release layer and extended release layer plus the claimed release controlling material(s) in the extended release layer. Saslawski et al. teach a multilayer tablet that can be made up of only two layers, i.e. a first layer (immediate or fast release layer) and second layer (prolonged release layer containing a nonbiodegradable, inert porous polymeric matrix). See page 2 lines 19-30. Saslawski et al. teach that both layers can contain the same active ingredient (page 4 lines 14-16). Saslawski et al. teach a wide selection of actives for the tablet including the instant nimesulide (naproxen). See page 4 line 14 - page 5 line 10. Saslawski et al. teach that fast and prolonged release layers can comprise wetting agents, pH regulators, lactose, starch, polyvinylidone, polyoxyethylene sorbitan monostearate, docusate sodium, magnesium stearate and croscarmellose. In addition to the above specified ingredients the prolonged release layer can comprise hydroxypropyl methylcellulose and sodium lauryl sulfate. See page 9 line 10 – page 12. Saslawski et al teach that the tablet can be polymer film coated (page 15 lines 3-6, page 19 lines 12-15). Saslawski et al. do not exemplify a tablet comprising specifically nimesulide as the active along with all of the ingredients listed above. However, Saslawski et al. do suggest such a combination of ingredients. Saslawski et al. also do not teach the tablet comprising colloidal silicone dioxide.

However, Gibson et al. teach that colloidal silicone dioxide is a common excipient used in immediate and controlled released tablet formulations (USPN '340 column 4 lines 47-60). Therefore, it would have been obvious to one having ordinary skill in the art to modify the invention of Saslawski et al. to include the silicone dioxide. One would have been motivated to do this since the silicone dioxide is a common excipient employed in immediate and control release formulations.

Response to Applicants Argument

Applicants argue that the cellulose polymers, carbomers, polyalkylene polyols, polycarbophils, gelatins and gums are sustain release biodegradable materials according to Chandra et al., Bernhard et al., and Ramakrishnan et al (References filed 4/24/09). The Examiner agrees that Chandra et al. reveal that methyl cellulose, ethyl cellulose, HPMC, HPC and cellulose acetate are biodegradable. However, the Examiner argues that Chandra et al. do not teach cellulose acetate butyrate, cellulose acetate propionate, cellulose acetate trimellitate are biodegradable. The Examiner agrees that Bernhard et al. teach that polyethylene glycols are biodegradable. However, the Examiner argues that Bernhard et al. do not suggest that the whole world of polyalkylene polyols is biodegradable. The Examiner agrees that Ramakrishnan et al. teach Gum Arabic is biodegradable. However, the Examiner argues that Ramakrishnan et al. do not suggest that the whole world of gums is biodegradable.

Therefore, the teaching of cellulose acetate butyrate, cellulose acetate propionate, cellulose acetate trimellitate, and the whole worlds of polyalkylene polyols and gums are biodegradable appears to be new matter.

Applicants argue that the combination of references do not disclose that the release control materials (ethyl cellulose and hydropropylmethyl cellulose) are biodegradable. The Applicants acknowledge that the combination of references suggest an invention that could comprise HPMC and/or EC. However, the Applicants point out that the HPMC suggested by the reference is a non-biodegradable binder or disintegrate rather than biodegradable control release agent as claimed. Applicants explain that biodegradable (control release agent) HPMC is distinguishable from non-biodegradable (binder or disintegrant) HPMC according to concentration, viscosity and molecular weight. The Applicants employ Sarfraz et al. and Rowe et al. to support the significances of HPMC viscosity in relation to whether HPMC behaves as a binder as opposed to a control release agent. If HPMC in the prior art's invention also acts a control releasing material producing the same benefit produced by the instant invention, the prior should have articulated the alternative including HPMC as a control release agent.

Applicants argue that the HPMC used in the instant invention has a concentration, viscosity and molecular weight that makes it control release agent rather than a binder or disintegrant. The Examiner argues that Applicants argue that both the prior art and instant invention teach the use of HPMC. The concentration of HPMC used in the prior art overlap with the amount used in the instant claims. For this reason, the Examiner argues that the HPMC in both the prior art and instant claims would yield the same function. Note, the instant claims state that the HPMC is biodegradable. However, the claims do not recite a viscosity range and/or molecular weight range for the HPMC

that distinguishes the prior art HPMC over the instant HPMC. In addition the ranges are also not recited in the instant specification. The Examiner has considered Sarfraz et al. and Rowe et al. and the Examiner maintains that the rejection of record makes the instant invention and claims obvious.

Nimesulide is not disclosed in WO '448. Nimesulide is distinct from Naproxen recited in the office action. Naproxen is not a NSAID compound like Nimesulide. The Examiner agrees with the Applicants' statement. However, it is important to note that WO '448 allows for the inclusion of NSAID compounds which would suggest the inclusion of Nimesulide (or the Sulfonanilide compound class). Although WO '448 does not specifically disclose Nimesulide or other sulfonanilides , WO '448 provides examples of NSAID compounds. Specifically note, WO '448 provides examples of NSAIDs such as or for example arylpropionic derivatives (page 5 lines 6-21). The use of the language such as/for example allows for the inclusion of NSAID compounds like Nimesulide which are not specifically recited in WO '448.

Applicants also argue that Nimesulide is a NSAID compound falling within the Sulfonanilide class. Although WO '448 discloses NSAID compounds, the reference does not recite the use of the sulfonanilide class of compounds like Nimesulide. WO '448 does not suggest the use of Nimesulide. The Examiner argues that WO '448 allows for the inclusion of NSAID compounds which would suggest the inclusion of Nimesulide (or the Sulfonanilide compound class). Although WO '448 does not specifically disclose Nimesulide or other sulfonanilides , WO '448 provides examples of NSAID compounds. Specifically note, WO '448 provides examples of NSAIDs such as or for example

arylpropionic derivatives (page 5 lines 6-21). The use of the language such as/for example allows for the inclusion of NSAID compounds like Nimesulide which are not specifically recited in WO '448.

Applicants use WO 91/17774, WO 99/41233, Nalluri et al and Piel et al to point out that Nimesulide is practically insoluble in water and difficult to formulate. On the other hand, instant invention provides a formulation for poorly water soluble nimesulide with release controlling materials. The Examiner argues that WO '448 at page 4 lines 17-38 to page 8 line 29 employ a wide range of active substances having a wide range of solubility properties – some soluble some insoluble, some showing pH-dependent solubility and some not showing pH-dependent solubility. The references referred to by the Applicants disclose that Nimesulide is practically insoluble in water. WO '448 teaching that a wide range of actives in terms of solubility properties can be employed makes it obvious to include the poorly water soluble nimesulide.

WO ‘448 does not disclose or suggest a once-a-day controlled release composition as recited in the amended claims. WO ‘448 shows composition dissolution in a max of 9 hours in the Figures. WO ‘448 does not disclose the materials that would prolong the release of the active substance for a longer period of time. The Examiner argues that WO '448 suggests the same combination of ingredients with NSAID compounds as recited in instant claims (see 103(a) rejection above). Therefore, it obvious that WO ‘448 yields a formulation that has prolonged release of the active. WO ‘448 does not have to exemplify all scenarios of the disclosed formulation in order to render instant once a day/prolonged formulation obvious.

WO ‘448 and USPN 6426340 do not make claimed invention obvious. USPN ‘340 discloses silicon as a common excipient employed in immediate and controlled release tablet formulation. USPN '340 does not teach multilayered or bilayered tablet of nimesulide as claimed in instant invention. The Examiner argues that USPN '340 is used for the sole purpose of showing that silicon dioxide is a common excipient used in immediate and controlled release tablet formulations.

The Applicants argue that the hydroxypropyl methylcellulose is used in the instant invention as a release controlling material, which is distinguished from the HPMC used in Saslawski et al as a disintegrant or as a binder rather than as a release rate controlling material as disclosed in the instant invention. Applicants provide literature by Rudnic et al. to support that a binder or disintegrating agent differs from a release controlling agent. The Examiner argues that HPMC is used in Saslawski et al. as well as in the instant in overlapping concentration ranges. Therefore, irrespective of what HPMC may be called it should render the same effect or benefit. The Examiner further argues that Saslawski et al. teach 0.5 to 25% wt binder such as HPMC (page 11 lines 25-28, page 12 lines 3-7), whereas the instant specification discloses 5-95% of a releasing agent such as HPMC (page 9, 2nd paragraph). Also note on page 5 of the specification 5 % to 65% of the release controlling agent (HPMC) is taught. Instant claim 2 teaches that the disintegrating agent (HPMC) ranges from 0 to 15% which overlaps the 5% to 65% amount taught at page 5 of the instant specification. Whether HPMC is called a sustained release material or a binder material is insignificant. The HPMC in

Saslawski et al and instant invention would be expected to yield the same effect or benefit since the inventions teach overlapping concentration ranges for HPMC.

The Applicants argue that Saslawski et al. uses specifically nonbiodegradable inert material in the second layer. Saslawski et al. do not teach or suggest the use biodegradable material in the second layer for the purpose of prolonging active NSAID (nimesulide). The terms nonbiodegradable and biodegradable adds no patentable weight to the instant claims since there is no recitation of either term in the claims. The instant claims do not make claim to nonbiodegradable material or biodegradable material. The Examiner acknowledges the references provided by the Applicants to support that instant release controlling materials are biodegradable. The Examiner reiterates that there is no recitation in the instant claims that the release controlling material is biodegradable.

The Applicants argue that Saslawski et al. do not teach nimesulide or any other sulfonanilide. Note, instant claims require the NSAID nimesulide. The Examiner argues while it is true that Saslawski et al do not teach nimesulide. Saslawski et al teach the NSAID naproxen. Skinhoj et al. teach use of both naproxen and nimesulide and suggest that both naproxen and nimesulide are equivalent. For this reason, it would have been obvious to artisan in the field to modify the invention of Saslawski et al. by substituting the naproxen taught therein with the nimesulide taught Skinhoj et al.

The Applicants argue that the Gibson reference cited in the office action has no relevance to the instant invention. Gibson mentions the use of silicon dioxide in immediate and controlled release formulation. The Examiner argues that the sole

purpose of employing Gibson was for the teaching that it is well known to use silicon dioxide in immediate and control release formulation.

Applicants argue that the prior art does not teach an invention comprising 200 mg micronized nimesulide having an average particle size below 5 microns. The Examiner argues that an artisan would have been motivated to determine the optimum amounts and particle size during routine experimentation. In the absence of unexpected data for the instant amount and particle size, the prior makes obvious the instantly claimed particle size and amounts.

The Examiner has considered Sarfraz et al. and Rowe et al. and the Examiner maintains that the rejection of record makes the instant invention and claims obvious

Applicants again refer the Examiner to a declaration showing results for the nimesulide 200 mg tablet in Example 10 with respect to efficacy, safety, osteoarthritis and sales. The Examiner reiterates that although the results may be true for the nimesulide 200 mg tablet in Example 10, the claims are not commensurate in scope with Example 10. In fact, Applicants do not provide any results for the tablet of claim 1 wherein nimesulide is present in both an immediate release layer and extended release layer. The extended release layer comprises one or more release controlling agent/material. For this reason the results provided by way of the declaration are not applicable for overcoming the rejection cited above. The Examiner reiterates that the claims are not commensurate in scope with tablet of Example 10.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,5,8-11,19 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Therefore the claim recitation of cellulose acetate butyrate, cellulose acetate propionate, cellulose acetate trimellitate, and the whole worlds of polyalkylene polyols and gums being biodegradable appears to be new matter.

Allowable Subject Matter

Claim 26 is allowable. See declaration dated 4/28/09.

Telephonic Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALTON N. PRYOR whose telephone number is (571)272-0621. The examiner can normally be reached on 8:00 a.m. - 4:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alton N. Pryor/
Primary Examiner, Art Unit 1616